IN THE DRAWINGS

The Examiner's approval of the correction of Figure 14(c) is requested, along with entry of the replacement drawing sheets submitted herewith.

REMARKS

Reconsideration and allowance are respectfully requested.

Claims 1, 4 and 6-9 are pending. The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. The limitations of dependent claims 3 and 5 are incorporated into independent claim 1.

From the original disclosure (e.g., specification and drawings), a person skilled in the art would readily appreciate what that the added reference numbers are proper. The brief description of the drawings is amended to refer to the numbers and to clarify what is illustrated in Figs. 1, 2 and 15.

As regards Fig. 4, Applicant submit that it is consistent with the description in the specification. As described therein, Figs. 4(a) and 4(b) are intended to be evidence for expression of a bFGF-displaying L protein and a BTC-displaying L protein. It should not be construed as evidence for expression of HBcAg. Therefore, Figs. 4(a) and 4(b) do not show expression of HBcAg (see also Example 4). The hollow nanoparticles used in the examples and described in the specification as made using the fungi mentioned in Examples 1 to 3. But in Example 4, the same fungi as in Examples 6 and 7 are used to produce the BTC-displaying HBsAg L particles and the bFGF-displaying HBsAg L particles, respectively. Figs. 14(c) and 11 clearly depict that the fungi express HBcAg. Thus, although Figs. 4(a) and 4(b) do not show expression of HBcAg, it should still clearly be understood from Figures 14(c), 11, etc. that the fungi used here express HBcAg.

With regard to the requirement to submit a drawing correction, replacement sheets with a corrected Figure 14(c) are submitted herewith. It would be appreciated from Example 7 of the original disclosure that lanes 1 and 2 of Fig. 14(c) show a BTC-displaying L protein. Also, a person skilled in the art would readily understand that the lower band in lane 1 show degradation products from the BTC-displaying L protein. It would also be appreciated from Example 7 that lanes 3 and 4 of Fig. 14(c) show an HBcAg protein.

Claim 1 was objected to. Its is amended to recite first and second proteins, which interact to form a capsid structure of the hollow nanoparticles. Applicants submit that the claim is clear. The plural form refers to a collection of more than one nanoparticles.

They may or may not be different from each other depending on the interaction between first and second proteins, and whether other components are present. In contrast to the allegation at page 3 of the Action, the plural form does not require a group of different nanoparticles that comprise different particle-forming first proteins. Withdrawal of the objections is requested.

35 U.S.C. 112 – Enablement

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 1-9 were rejected under Section 112, first paragraph, because they allegedly contain "subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Applicants traverse.

A person skilled in the art would readily appreciate from the original disclosure that the first protein comprises a hepatitis B virus surface-antigen protein whose hepatocyte recognition site is modified to another bio-recognizing molecule and the second protein comprises a hepatitis B virus core-antigen protein interact with each other when the two proteins are coexpressed. For example, Figs. 12(a), 12(b), 13(a), 13(b) and 13(c) show experimental results with bFGF-displaying HBsAg L particles which is an example of the hollow nanoparticles of the present invention. The results of CsCl density-gradient centrifugation shown in the drawings indicate that the bFGF fusion L protein and the HBcAg protein were detected in the same fraction. A person skilled in the art would understand from these facts that the bFGF fusion L protein and the HBcAg protein interact at least partially with each other in accordance with the requirement

from claim 1 that "at least one of the first proteins interacts with a second protein" to form a capsid structure.

In addition, Figs. 14(b) and 14(c) show similar experimental results with BTC-displaying HBsAg L particles. This is another example of the hollow nanoparticles of the present invention. These results indicate that the BTC fusion L protein and the HBcAg protein interact at least partially with each other.

The aforementioned is evidence that Applicants indeed verified through experimentation that the bFGF fusion L protein and the HBcAg protein interact at least partially with each other, and that the BTC fusion L protein and the HBcAg protein interact at least partially with each other.

It is a well-known fact to a person skilled in the art that the HBcAg protein forms a capsid structure.

The bFGF fusion L protein and the BTC fusion L protein are L proteins whose hepatocyte recognition site is modified. The hepatocyte recognition site corresponds to an extracellular domain of the HBsAgL protein.

It is also well-known to a person skilled in the art that the domain corresponding to bFGF and the domain corresponding to BTC, both in the fusion L protein, entirely differ from each other if analyzed down to the amino acid level. Applicants' specification describes both fusion L proteins as having totally different amino acid sequences substituted at hepatocyte recognition sites interacting with the HBcAg protein. In other words, Applicants' specification describes that it is the amino acid sequence except for the heaptocyte recognition site (e.g., intracellular domain of the L protein) that is important to the interaction of the fusion L protein and the HBcAg protein.

Claim 1's first protein is a hepatitis B virus surface-antigen protein whose hepatocyte recognition site is modified to another bio-recognizing molecule. The amino acid sequence except for the hepatocyte recognition site of the first protein is basically conserved. In addition, claim 1's second protein is a hepatitis B virus core-antigen protein. Applicants therefore submit that the presently claimed invention satisfies the requirements set forth in Section 112, first paragraph.

Withdrawal of the enablement rejection made under Section 112, first paragraph, is requested because it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 1-2 and 5-9 were rejected under Section 102(b) as allegedly anticipated by Shiosaki et al. (Gene 106:143-149, 1991). Applicants traverse because the limitation of claim 3 was incorporated into claim 1. Claim 3 was not subject to this rejection. Thus, independent claim 1 and claims depending therefrom are not anticipated by Shiosaki et al. because they are novel over the prior art.

Withdrawal of the Section 102 rejection is requested because the cited document fails to disclose all limitations of the claimed invention.

Conclusion

Having fully responded to all of the pending objections and rejections contained in this Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect.

Respectfully submitted,

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By: _____

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